



King's Research Portal

DOI:

[10.1017/S0033291715001816](https://doi.org/10.1017/S0033291715001816)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Ajnakina, O., Trotta, A., Oakley-Hannibal, E., Di Forti, M., Stilo, S. A., Kolliakou, A., Gardner-Sood, P., Gaughran, F., David, A. S., Dazzan, P., Pariante, C., Mondelli, V., Morgan, C., Vassos, E., Murray, R. M., & Fisher, H. L. (2016). Impact of childhood adversities on specific symptom dimensions in first-episode psychosis. *Psychological Medicine*, 46(2), 317-326. <https://doi.org/10.1017/S0033291715001816>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Impact of childhood adversities on specific symptom dimensions in first-episode psychosis

Olesya Ajnakina¹, Antonella Trotta¹, Elizabeth Oakley-Hannibal¹, Marta Di Forti^{2,3}, Simona A. Stilo¹, Anna Kolliakou⁴, Poonam Gardner-Sood¹, Fiona Gaughran^{1,3}, Anthony S. David^{1,3}, Paola Dazzan^{1,3}, Carmine Pariante^{3,4}, Valeria Mondelli^{3,4}, Craig Morgan^{3,5}, Evangelos Vassos², Robin M. Murray^{1,3}, Helen L. Fisher^{*2}

¹Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. ²MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. ³National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, London, UK. ⁴Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. ⁵Centre for Epidemiology and Public Health, Health Service & Population Research Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

*Address for correspondence: Dr Helen L. Fisher, MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 16 De Crespigny Park, London, SE5 8AF, UK. (Email: helen.2.fisher@kcl.ac.uk)

Financial Support

This study was funded by the United Kingdom National Institute of Health Research Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust; the Institute of Psychiatry, Psychology & Neuroscience at King's College London; The Psychiatry Research Trust; and the Maudsley Charitable research fund. Dr Fisher is supported by a Fellows Award from the MQ: Transforming Mental Health charity (grant number: MQ14F40).

Abstract

Background. The relationship between childhood adversity (CA) and psychotic disorder is well documented. As the adequacy of the current categorical diagnosis of psychosis is being increasingly questioned, we explored independent associations between different types of CA and specific psychotic symptom dimensions in a well-characterised sample of first-episode psychosis (FEP) patients.

Methods. This study involved 236 FEP cases aged 18 to 65 years who presented for the first time to psychiatric services in South London, UK. Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) and confirmatory factor analysis was used to evaluate the statistical fit of the Wallwork/Fortgang five-factor model of psychosis. CA prior to 17 years of age (physical abuse, sexual abuse, parental separation, parental death, and being taken into care) was retrospectively assessed using the Childhood Experience of Care and Abuse Questionnaire (CECA.Q).

Results. Childhood sexual abuse ($\beta=0.96$, 95% CI 0.40-1.52), childhood physical abuse ($\beta=0.48$ 95% CI 0.03-0.93) and parental separation ($\beta=0.60$ 95% CI 0.10-1.11) showed significant associations with the positive dimension; while being taken into care was associated with the excited dimension ($\beta=0.36$, 95% CI 0.08-0.65), independent of the other types of CA. No significant associations were found between parental death and any of the symptom dimensions.

Conclusions. A degree of specificity was found in the relationships between different types of CA and psychosis symptom dimensions in adulthood suggesting that distinct pathways may be involved in the CA-psychosis association. These potentially different routes to developing psychosis merit further empirical and theoretical exploration.

Key words: child abuse; dimensions; factor analysis; first-episode psychosis; maltreatment.

Introduction

The prevalence of adverse childhood events, such as childhood sexual abuse (CSA) or childhood physical abuse (CPA), in the general public is surprisingly high with estimates of up to a quarter of all children affected in high-income countries (Gilbert *et al.* 2009; Radford *et al.* 2013). CSA and CPA are often considered the most toxic forms of childhood adversity (CA); though in recent years, death of a significant other, separation from a parent-figure and placement in institutional care during early childhood have also been recognised as having detrimental consequences for mental health (Read *et al.* 2005; Morgan *et al.* 2007; Read & Bentall, 2012). Some have attempted to claim that, assuming causality, one-third of new cases of psychotic disorders may be attributable to CA (Dvir *et al.* 2013).

Despite this intriguing research, pathogenic mechanisms that link CA to psychotic disorders are not well understood (Bentall *et al.* 2014). This may be due to existing studies predominantly utilising the traditional diagnostic categories of psychosis, the adequacy of which has increasingly been questioned (Costello, 1992; van Os *et al.* 1999; Cuthbert, 2014). Instead it has been postulated that the phenomenology of psychosis may be better conceptualised by symptom dimensions (Kay & Sevy, 1990; van Os *et al.* 1996; van Os *et al.* 1999). The importance of symptom profiles (van Os *et al.* 1999; Dikeos *et al.* 2006) and their superiority over diagnostic categories at predicting clinical course and outcome of psychosis has been demonstrated (van Os *et al.* 1996; Demjaha *et al.* 2009). In terms of research into the associations between CA and psychosis, application of symptom dimensions may increase the statistical power to detect associations over categories especially where the categories may lack validity. However, research conducted in first-episode psychosis (FEP) cases where symptomatology is not affected by differences in clinical practice, hospitalisation and treatment choices is still lacking (Emsley *et al.* 2003; Demjaha *et al.* 2009). Existing research has most frequently identified multidimensional models with five factors (Bell *et al.* 1994; Lindenmayer *et al.* 1994; White *et al.* 1997; Lancon *et al.* 1998; Emsley *et al.* 2003). Based on previous work, Wallwork *et al.* (2012) derived a

consensus five-factor model of psychosis that comprised positive (e.g., delusions, hallucinatory behaviour), negative (e.g., blunted affect, emotional withdrawal), disorganised/concrete (e.g., conceptual disorganisation, difficulty in abstract thinking), excited (e.g., excitement, hostility) and depressed (e.g., depression, guilt feelings) dimensions. This Wallwork/Fortgang five-factor model has been shown to be the most robust PANSS factorial solution for exploring symptom profiles in first-episode psychosis patients (Langeveld *et al.* 2013) and thus is the factorial model we chose to utilise in the current study.

In the present study we conducted confirmatory factor analyses (CFA) of the Wallwork/Fortgang five-factor model (Wallwork *et al.* 2012) using data from a relatively large and well-characterised sample of patients presenting to psychiatric services for the first time with psychosis. We then aimed to examine independent associations between different types of CA (physical abuse, sexual abuse, parental separation, parental death, and being taken into care) and each of these specific psychotic symptom dimensions. Previously an association of childhood trauma with psychotic disorder has been demonstrated in this sample (Trotta *et al.* 2015). Given previous research that has explored associations between CA and individual symptoms of psychosis and schizotypy, we hypothesised that all forms of CA would be associated with the positive dimension (Read *et al.* 2003; Janssen *et al.* 2004; Whitfield *et al.* 2005; Schürhoff *et al.* 2009; Bentall *et al.* 2012; Stilo *et al.* 2013; Velikonja *et al.* 2015). As there is a consistent body of literature linking CSA with depression (e.g., Bifulco *et al.* 1991; Kendler & Aggen, 2014; Sitko *et al.* 2014) we also hypothesised that this type of CA would be associated with the depressed symptom dimension.

Methods

Sample

Participants were recruited as part of the Biomedical Research Centre (BRC) Genetics and Psychosis (GAP) study, a large case-control study conducted in South London, UK. The

study included patients aged 18 to 65 years who presented to psychiatric wards in the South London and Maudsley National Health Service (NHS) Foundation Mental Health Trust between January 2006 and October 2010 with a first episode of psychosis (International Classification of Diseases [ICD-10] codes F20-F29 and F30-F33) (World Health Organisation [WHO], 1992). Exclusion criteria were: 1) evidence of psychotic symptoms precipitated by an organic cause; 2) transient psychotic symptoms resulting from acute intoxication as defined by ICD-10; 3) head injury causing clinically significant loss of consciousness; 4) under the age of 18 or over 65; and 5) learning disability (IQ<70). The original GAP sample comprised 339 FEP patients; of these symptom data were available for 236 patients (69.6% of the original GAP sample). Therefore, the data we present here are based on these 236 patients for whom we had complete symptom data.

Ethics

The GAP study was granted ethical approval by the South London and Maudsley and Institute of Psychiatry Local Research Ethics Committee (reference number: 05/Q0706/158). All cases gave informed written consent after reading a detailed information sheet.

Assessments

Socio-demographic characteristics. The Medical Research Council (MRC) Socio-demographic Schedule modified version was utilised to collect data on socio-demographic characteristics (Mallett *et al.* 2002). Ethnicity was self-ascribed using the 16 categories employed by the 2001 UK Census (<http://www.ons.gov.uk/ons/guide-method/census/census-2001/index.html>). Due to small numbers in some ethnic categories, we combined them into three broad ethnic groups: White (all white groups), Black (all black groups), and Other (encompassing Asian, mixed-ethnicity and other ethnicities). Lifetime history of alcohol use prior to the onset of psychosis was collated using the Alcohol Use Disorders Identification Test (AUDIT; Babor *et al.* 1989) and was split into ever used alcohol (1) versus never used alcohol (0). Lifetime use of cannabis and other illegal substances prior

to the onset of psychosis was assessed with the Cannabis Experience Questionnaire modified version (Di Forti *et al.* 2009). Patients were divided into those who reported ever having used cannabis (1) and those who reported never having used it (0). Similarly, use of any other illegal substances was coded as ever used (1) versus never used (0). The Family Interview for Genetic Studies (FIGS; <https://www.nimhgenetics.org/interviews/figs>) and clinical records were used to obtain information about patients' family history of mental health problems. A family history of psychosis variable was derived following consensus diagnoses based on the available information and referred to the presence (1) or absence (0) of a current or past psychotic disorder in at least one first-degree relative.

Clinical presentation. Duration of untreated psychosis (DUP) was determined from the assessment interview and mental health records and defined as the difference between the date of the appearance of the first positive psychotic symptom (hallucination, delusion or thought disorder rated as 4 or higher on the Positive and Negative Syndrome Scale (PANSS; Kay *et al.* 1987) as per Singh *et al.* 2005) and date of first contact with mental health services for psychosis (Morgan *et al.* 2006). Diagnoses were made from interviews and mental health records utilising the Operational Criteria Checklists (OPCRIT) (McGuffin *et al.* 1991). In the present study, diagnoses were grouped using ICD-10 codes into schizophrenia-spectrum (F20-29), affective psychoses (F30.2, F31.2, F31.5, F32.3 or F33.3) and other psychoses (F10, F53).

Childhood adversity. CA was assessed using the Childhood Experience of Care and Abuse Questionnaire (CECA.Q; Bifulco *et al.* 2005), which was read out to participants during a face-to-face interview. The CECA.Q is a self-report instrument developed to retrospectively assess CA that occurred before 17 years of age. In this study, the focus was on five forms of CA that have been proposed to play an important role in the aetiology of psychosis: i) physical abuse inflicted by either one or both parent-figures; ii) sexual abuse perpetrated by an individual at least 5 years older than the victim; iii) separation from either or both parent-

figures for a period of at least 6 months; iv) death of either or both parent-figures; and v) being taken into care by the authorities. Full details of this measure are provided elsewhere (Bifulco *et al.* 2005; Fisher *et al.* 2010). Briefly, the CPA and CSA sections begin with screening questions where the positive responses are followed up with more detailed questions. In order to establish the severity of CPA experienced, the 4 follow-up questions are designed to elicit more detailed information on the frequency of attacks, severity of the injuries sustained and whether the perpetrator was out of control. For CSA, the 7 additional probes inquire about degree of sexual contact, relationship to perpetrator, and frequency of occurrence. The items for each type of abuse are summed separately to obtain a total CPA score and a total CSA score. Full scoring guidance and a copy of the measure are available at www.cecainterview.com. To ensure that the CECA.Q scores reflected a reasonable level of severity in the analysis, the total scores for the CPA and CSA subscales were dichotomised using the most conservative published cut-points (Bifulco *et al.* 2005). This measure has been shown to have good psychometric properties in patients with psychosis (Fisher *et al.* 2011).

Psychotic symptoms. The Positive and Negative Syndrome Scale (PANSS; Kay *et al.* 1987) was completed in face-to-face interviews with the patients to assess psychotic symptoms over the week preceding the assessment. The 30 items are each rated on a 7-point scale (1=absent, 7=extreme) and grouped into three subscales: positive symptoms (7 items), negative symptoms (7 items) and general psychopathology (16 items).

Analysis

All analyses were conducted in STATA release 12 (STATACorp LP, USA). Confirmatory factor analysis (CFA) was conducted to evaluate the statistical fit (Stefanovics *et al.* 2014) of the Wallwork/Fortgang five-factor model of psychosis (Wallwork *et al.* 2012) in this sample of patients with FEP. This model comprises *positive* (i.e., P1, P3, P5, G9), *negative* (i.e., N1, N2, N3, N4, N6 and G7), *disorganised/concrete* (i.e., P2, N5, G11), *excited* (i.e., P4, P7, G8

and G14) and *depressed* (i.e., G2, G3 and G6) factors. The factors identified by the Wallwork/Fortgang five-factor model were entered as latent variables in the CFA and the PANSS items were entered as observed variables. The Goodness-of-Fit Index statistics were used to determine the adequacy of fit of the model. These included the comparative fit index (CFI; values greater than 0.90 indicate good model fit), the root mean square error of approximation (RMSEA; values less than 0.06 indicate good model fit), and the standardised root mean square residual (SRMR; values less than 0.08 indicate good model fit) (Stefanovics *et al.* 2014). To assess the improvement in the fit of the model, correlated measurement errors were introduced into the model based on significantly correlated residuals indicated by modification indices (Liemburg *et al.* 2013).

Following CFA, factor scores for each of the five symptom dimensions were calculated for each patient using STATA's 'predict' post-estimation command. The distributions of the obtained symptom dimensions were examined and found to be normally distributed (see Supplementary Figures 1-5) thus meeting criteria for linear regression analysis. Linear regression was utilised to examine associations between each type of CA and the continuous symptom dimension scores. This set of analyses was controlled for age at first contact with mental health services for psychosis, gender, ethnicity, lifetime use of alcohol, cannabis or other illegal substances prior to psychosis onset, and family history of psychosis. To explore whether the relationships were independent of the effects of other forms of CA, the identified significant associations were re-examined additionally controlling for the other types of CA.

Results

Sample characteristics

Of the patients recruited to the GAP study ($N=339$), the PANSS was completed for 236 patients (69.6%). This subsample with PANSS ratings did not differ significantly from the full GAP sample in terms of gender ($\chi^2=0.41$ $p=0.52$), ethnicity ($\chi^2=3.29$ $p=0.19$) and duration of

untreated psychosis (DUP_{days}) ($t=0.37$ $p=0.99$); though, those patients without the PANSS tended to be older ($t=1.97$ $p=0.05$) (Supplementary Table 1).

Data on demographic characteristics, clinical presentation and prevalence of CA for our sample are presented in **Table 1**. The mean age at first contact was 29 years ($SD=9.1$) and the majority of the sample were men (64.8%). Around a third (35.2%) was of white and 40.2% of black ethnicity. Just over two-thirds of the cases were diagnosed with schizophrenia-spectrum disorders (68.8%) and a quarter with affective psychoses (26.8%). The most common type of CA reported was separation from one or both parent-figures (34.9%), followed by CPA (27.2%). Being placed into care by the authorities before 17 years of age was the least prevalent adversity (9.6%).

Confirmatory factor analysis

CFA was conducted in the current sample with the Wallwork/Fortgang five-factor model of PANSS items. The mean and standard deviation (SD) of the actual PANSS scores are presented in Supplementary Table 2. When the correlated residuals (i.e., measurement errors) were not introduced into the model the results of the CFA indicated a poor model fit: $CFI=0.767$, $RMSEA=0.101$ (95% CI 0.092-0.111) and $SRMR=0.111$. However, once significantly correlated residuals were incorporated into the model, the CFA produced an excellent fit of the model: the $CFI=0.959$, $RMSEA=0.052$ (95% CI 0.037-0.067) and $SRMR=0.071$. Scores for all five symptom dimensions appeared to be normally distributed (Supplementary Figures 1-5).

Average symptom dimension scores by type of CA

The mean symptom dimension scores for each of the five types of CA are illustrated in **Figure 1**. Those patients who reported parental separation, relative to those who did not experience this type of CA, had a higher mean score for the positive dimension. Similarly, those patients who reported CSA and those who reported CPA had higher mean scores for

the positive symptom dimension as well as lower mean scores for the negative symptom dimension compared to patients who did not report these forms of CA. Apart from the depressed dimension, the severity of the other four symptom dimensions was more pronounced among those who were placed in institutional care before age 17 compared to those who were not. This was particularly the case for the positive and disorganised/concrete dimensions. Among those who had one or both parents die before they turned 17, the mean score for the disorganised/concrete dimension was slightly higher than for those patients who did not experience parental loss.

Associations between CA and symptom dimensions

Unstandardized betas from regression analyses of the associations between each type of CA and symptom dimension scores are shown in **Table 2**. There was a significant association between CSA and the positive dimension indicating that those individuals who experienced this form of CA scored on average 0.90 higher on the positive dimension than those who did not report CSA. Similarly, there was a significant but substantially weaker association of CSA with the excited dimension ($\beta=0.22$). Although neither of the 95% confidence intervals (CIs) for these associations contained the point estimate of the other association, there was some overlap between the CIs indicating that CSA could not be said to be independently associated with both the positive and excited dimension. Reported exposure to CPA was associated with significant increases in average scores on the positive, disorganised/concrete and excited symptom dimensions compared to those who did not report this form of CA. However, the CIs for these associations overlapped and contained the point estimates thus suggesting that CPA was not independently associated with these three symptoms dimensions. Those who were taken into care showed an average increase of 0.49 on the disorganised/concrete and 0.40 on the excited dimensions compared to those patients who did not report this form of CA. Again there was no evidence of independent associations with these two symptom dimensions. Additionally, experience of

parental separation was associated with a significant increase of 0.51 in the average score on the positive dimension.

To explore whether these significant associations were truly independent of the effects of other forms of CA, each significant relationship was re-analysed additionally controlling for the remaining types of CA. The relationship between parental separation and the positive symptom dimension remained significant ($\beta=0.60$ 95% CI 0.10-1.11). Although the magnitude of the relationship between CPA and the positive dimension weakened it remained significant ($\beta=0.48$, 95% CI 0.03-0.93). The association of CSA with the positive dimension was also robust to adjustment for other types of CA and remained significant ($\beta=0.96$, 95% CI 0.04-0.64). Finally, the association between being taken into care and the excited dimension retained significance ($\beta=0.36$, 95% CI 0.08-0.65). All other associations were attenuated and failed to reach conventional 0.05 level of statistical significance.

Discussion

In the present study of first-episode psychosis patients we have identified independent and robust associations between three forms of childhood adversity, CSA, CPA and parental separation, and the positive psychosis symptom dimension from the Wallwork/Fortgang five-factor consensus model of psychosis. Additionally, placement in institutional care before the age of 17 was significantly associated with the excited dimension, independent of the other forms of adversity. However, no significant associations were found between parental death and any of the symptom dimensions.

Methodological considerations

A major strength of the current study is that it is the first study to have examined the relationships between several specific forms of CA and symptom dimensions in a sample of first-episode psychosis patients. The five factor model of psychosis symptoms employed in the present study was selected for being a “consensus” model derived from existing studies

(Wallwork *et al.* 2012) that has been shown to be optimal for use in FEP samples (Langeveld *et al.* 2013). This will likely facilitate the comparability of our results with those obtained in future studies. The symptom dimensions were founded on the PANSS which has previously been shown to be resilient to the effects of age, severity of symptoms, chronicity of illness (White *et al.* 1997) and short-term medication withdrawal (Lindenmayer *et al.* 1994). Moreover, the sample utilised in the present study was a well-characterised sample of recent-onset patients presenting for the first time with psychosis and thus the findings are not confounded by chronicity of illness or prolonged medication use. Additionally, the regression analyses were controlled for important confounding factors, such as substance use and genetic risk (Sideli *et al.* 2012) in addition to age at first contact with mental health services for psychosis, gender and ethnicity. Therefore, we can be more certain that the identified relationships are independent of the effects of these potentially confounding factors.

However, several methodological issues should be considered when interpreting the results of this study. Retrospective accounts of CA were utilised which could be biased due to forgetting over time and the reality distortions experienced by many patients with psychosis (Garety *et al.* 2001; Lysaker *et al.* 2005; Bendall *et al.* 2008; Vassos *et al.* 2008). However, reports of CA obtained retrospectively from individuals with psychotic disorders have been shown to be stable over time and unaffected by severity of psychotic or affective symptoms (Fisher *et al.* 2011). Secondly, as we did not have PANSS scores for the whole sample it is possible that this may have led to results being affected by selection bias. However, the comparison analyses between the full GAP sample and the subsample with PANSS ratings did not uncover any indication of potential biases. It is also noteworthy that the PANSS covered only 1 week of symptoms prior to the interview and thus may not be able to provide the best indicator of the overall clinical profile of these patients. Finally, the number of statistical tests carried out was significantly substantial; thus we cannot confidently rule out the possibility that some of associations might have been due to type I errors.

Childhood adversity and symptom dimensions

Previously, a 3-fold-increase in odds of psychosis in those who had reported a history of death of a parent during childhood has been reported (Stilo *et al.* 2013). In the present study, though, this type of CA was not associated with specific symptom dimensions. However, the association of CSA with the positive dimension was noticeably strong. Population-based studies have demonstrated that CSA is strongly related to delusions (Janssen *et al.* 2004) and hallucinations (Sitko *et al.* 2014), though this finding is not consistent across all studies (Read *et al.* 2005). Similarly, there was a robust significant association between parental separation and the positive symptom dimension. The pathogenic mechanism underlying these relationships could be explained in terms of attachment theory (Levy, 2013). Accordingly, CSA and prolonged separation from parents may be considered as a profound failure to provide the security required for development of a secure attachment triggering intense fears and profound anxieties (Smith *et al.* 2012). These in turn have been linked to emotional over-reactivity to stressful external stimuli (Collip *et al.* 2008) leading to impaired rational cognition (Garety *et al.* 2001) and increased paranoid thoughts (Sitko *et al.* 2014; Wickham *et al.* 2015). Additionally, parental separation during the early years of childhood is also tied to other important adverse experiences, such as family conflict, financial burden and neglect (Rutter, 2006), which may be risk factors increasing vulnerability to positive symptoms of psychosis. Furthermore, a significant relationship between CPA and the positive dimension of psychosis may indicate that a constant anticipation of threat or violence may lead to the onset of delusions, unusual thought processes and hallucinations (Bentall *et al.* 2008).

In our study we found a significant association between being taken into care and the excited symptom dimension. This is consistent with previous research indicating associations between childhood maltreatment and the onset of symptoms related to this dimension (Gilman *et al.* 2015) and bipolar disorder (Fisher & Hosang, 2010). Although we

did not find independent associations between other forms of adversity and the excited dimension in this study, it is possible that being taken into care represents the more severe end of the spectrum of physical and sexual abuse and/or is capturing extreme experiences of neglect. Indeed CSA and CPA were initially associated with the excited dimension but these relationships were attenuated when controlling for being taken into care (and the other adversities) indicating some overlap between them. Behavioural traits such as hostility, lack of impulse control and uncooperativeness, that comprised the excited dimension, may have developed due to these institutionalised children being brought up in a less structured environment. Indeed around two-thirds of youths in one local British child welfare authority met criteria for conduct disorder (McCann *et al.* 1996). These behavioural problems could also have been the outcome of an abusive or neglectful family environment (Jaffee *et al.* 2004; Sarchiapone *et al.* 2009). Either way, previous research has shown that maltreatment that comes to the attention of social services (which is likely to result in being taken into care) is associated with antisocial and impulsive behaviour (Cohen *et al.* 2001), that may have been captured by the excited dimension in this study. It will be important to explore in other samples whether a similar association is evident in order to rule out the possibility that our finding was a statistical artefact.

Conclusion

It has been demonstrated that physical abuse, sexual abuse, parental separation and being taken into care before 17 years of age exhibited associations with particular symptom dimensions of psychosis in adulthood independent of important confounding factors and the other types of adversity investigated. These findings add further weight to the suggestion that there may be distinct pathways from specific forms of CA to particular types of psychotic symptoms (Bentall *et al.* 2014) and these warrant further investigation. In terms of clinical implications, our findings reiterate the need for a history of childhood adversity to be taken during routine psychiatric assessments of individuals presenting with psychosis in order to facilitate meaningful and comprehensive treatment plans (Read & Bentall, 2012). Eventually,

these findings might also feed into interventions targeting high-risk children. However, it remains to be determined whether the present findings can be replicated in other first-episode psychosis samples when controlling for all potential confounders.

Acknowledgements

The patients included in the present study were recruited in collaboration with the GAP and PUMP study teams and the South London and Maudsley (SLaM) NHS Foundation Trust. We would like to thank all of the patients who gave up their time to take part in this study and all of the staff and students who worked tirelessly to collect the data. This paper summarises independent research funded by the National Institute for Health Research (NIHR) under its IMPACT Programme (Grant Reference Number RP-PG-0606-1049). The views expressed are those of the author(s) and not necessarily those of the National Health Service (NHS), the NIHR or the Department of Health.

Declaration of Interest

R.M. Murray has received honoraria from Janssen, Astra-Zeneca, Lilly, BMS, and is an editor of this journal. A.S. David has received honoraria from Janssen and Roche Pharmaceuticals. Fiona Gaughran has received honoraria for advisory work and lectures from Roche, BMS, Lundbeck, and Sunovion and has a family member with professional links to Lilly and GSK.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

- Babor TF, de la Fuente JR, Saunders J, Grant M** (1992). *AUDIT. The Alcohol Use Disorders Identification Test. Guidelines for use in primary health care*. World Health Organisation: Geneva, Switzerland.
- Bell MD, Lysaker PH, Beam-Goulet JL, Milstein RM, Lindenmayer JP** (1994). Five-component model of schizophrenia: assessing the factorial invariance of the positive and negative syndrome scale. *Psychiatry Research* **52**, 295-303.
- Bendall S, Jackson HJ, Hulbert CA, McGorry PD** (2008). Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. *Schizophrenia Bulletin* **34**, 568-579.
- Bentall R, de Sousa P, Varese F, Wickham S, Sitko K, Haarmans M, Read J** (2014). From adversity to psychosis: pathways and mechanisms from specific adversities to specific symptoms. *Social Psychiatry and Psychiatric Epidemiology* **49**, 1011-1022.
- Bentall RP, Rowse G, Kinderman P, Blackwood N, Howard R, Moore R, Cummins S, Corcoran R** (2008). Paranoid delusions in schizophrenia and depression: the transdiagnostic role of expectations of negative events and negative self-esteem. *Journal of Nervous & Mental Disease* **196**, 375–383.
- Bentall RP, Wickham S, Shevlin M, Varese F** (2012). Do specific early-life adversities lead to specific symptoms of psychosis? A study from the 2007 the Adult Psychiatric Morbidity Survey. *Schizophrenia Bulletin* **38**, 734-740.
- Bifulco A, Bernazzani O, Moran PM, Jacobs C** (2005). The childhood experience of care and abuse questionnaire (CECA.Q): validation in a community series. *British Journal of Clinical Psychology* **44**, 563-581.
- Bifulco A, Brown GW, Adler Z** (1991). Early sexual abuse and clinical depression in adult life. *British Journal of Psychiatry* **159**, 115-122.

Cohen P, Brown J, Smaile E (2001). Child abuse and neglect and the development of mental disorders in the general population. *Development & Psychopathology* **13**(4), 981-999.

Collip D, Myin-Germeys I, van Os J (2008). Does the concept of "sensitization" provide a plausible mechanism for the putative link between the environment and schizophrenia? *Schizophrenia Bulletin* **34**, 220-225.

Costello CG (1992). Research on symptoms versus research on syndromes. Arguments in favour of allocating more research time to the study of symptoms. *British Journal of Psychiatry* **160**, 304-308.

Cuthbert BN (2014). The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *World Psychiatry* **13**, 28-35.

Demjaha A, Morgan K, Morgan C, Landau S, Dean K, Reichenberg A, Sham P, Fearon P, Hutchinson G, Jones PB, Murray RM, Dazzan P (2009). Combining dimensional and categorical representation of psychosis: the way forward for DSM-V and ICD-11? *Psychological Medicine* **39**, 1943-1955.

Di Forti M, Morgan C, Dazzan P, Pariante C, Mondelli V, Marques TR, Handley R, Luzzi S, Russo M, Paparelli A, Butt A, Stilo SA, Wiffen B, Powell J, Murray RM (2009). High-potency cannabis and the risk of psychosis. *British Journal of Psychiatry* **195**(6), 488-491.

Dikeos DG, Wickham H, McDonald C, Walshe M, Sigmundsson T, Bramon E, Grech A, Touloupoulou T, Murray R, Sham PC (2006). Distribution of symptom dimensions across Kraepelinian divisions. *British Journal of Psychiatry* **189**, 346-353.

Dvir Y, Denietolis B, Frazier JA (2013). Childhood trauma and psychosis. *Child and Adolescent Psychiatric Clinics* **22**, 629-641.

Emsley R, Rabinowitz J, Torremans M (2003). The factor structure for the Positive and Negative Syndrome Scale (PANSS) in recent-onset psychosis. *Schizophrenia Research* **61**, 47-57.

Fisher HL, Craig TK, Fearon P, Morgan K, Dazzan P, Lappin J, Hutchinson G, Doody GA, Jones PB, McGuffin P, Murray RM, Leff J, Morgan C (2011). Reliability and comparability of psychosis patients' retrospective reports of childhood abuse. *Schizophrenia Bulletin* **37**, 546-553.

Fisher HL, Hosang GM (2010). Childhood maltreatment and bipolar disorder: a critical review of the evidence. *Mind & Brain: The Journal of Psychiatry* **1(1)**, 75-85.

Fisher HL, Jones PB, Fearon P, Craig TK, Dazzan P, Morgan K, Hutchinson G, Doody GA, McGuffin P, Leff J, Murray RM, Morgan C (2010). The varying impact of type, timing and frequency of exposure to childhood adversity on its association with adult psychotic disorder. *Psychological Medicine* **40**, 1967-1978.

Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine* **31**, 189-195.

Gilbert R, Widom CS, Browne K, Fergusson D, Webb E, Janson S (2009). Burden and consequences of child maltreatment in high-income countries. *Lancet* **373**, 68-81.

Gilman SE, Ni MY, Dunn EC, Breslau J, McLaughlin KA, Smoller JW, Perlis RH (2015). Contributions of the social environment to first-onset and recurrent mania. *Molecular Psychiatry* **20(3)**, 329-336.

Jaffee SR, Caspi A, Moffitt TE, Taylor A (2004). Physical maltreatment victim to antisocial child: evidence of an environmentally mediated process. *Journal of Abnormal Psychology* **113(1)**, 44-55.

Janssen I, Krabbendam L, Bak M, Hanssen M, Vollebergh W, de Graaf R, van Os J (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica* **109**, 38-45.

Kay SR, Fiszbein A, Opler LA (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* **13**, 261-276.

Kay SR, Sevy S (1990). Pyramidal model of schizophrenia. *Schizophrenia Bulletin* **16**, 537-545.

Kendler KS, Aggen SH (2014). Clarifying the causal relationship in women between childhood sexual abuse and lifetime major depression. *Psychological Medicine* **44**, 1213-1221.

Lancon C, Aghababian V, Llorca PM, Auquier P (1998). Factorial structure of the Positive and Negative Syndrome Scale (PANSS): a forced five-dimensional factor analysis. *Acta Psychiatrica Scandinavica* **98**, 369-376.

Langeveld J, Andreassen OA, Auestad B, Færden A, Hauge LJ, Joa I, Johannessen JO, Melle I, Rund BR, Røssberg JI, Simonsen E, Vaglum P, Larsen TK (2013). Is there an optimal factor structure of the Positive and Negative Syndrome Scale in patients with first-episode psychosis? *Scandinavian Journal of Psychology* **54**, 160-165.

Levy KN (2013). Introduction: attachment theory and psychotherapy. *Journal of Clinical Psychology* **69**, 1133-1135.

Liemburg E, Castelein S, Stewart R, van der Gaag M, Aleman A, Kneegtering H (2013). Two subdomains of negative symptoms in psychotic disorders: established and confirmed in two large cohorts. *Journal of Psychiatric Research* **47**, 718-725.

Lindenmayer JP, Bernstein-Hyman R, Grochowski S (1994). A new five factor model of schizophrenia. *Psychiatric Quarterly* **65**, 299-322.

Lysaker PH, France CM, Hunter NL, Davis LW (2005). Personal narratives of illness in schizophrenia: associations with neurocognition and symptoms. *Psychiatry* **68**, 140-151.

Mallett R, Leff J, Bhugra D, Pang D, Zhao JH (2002). Social environment, ethnicity and schizophrenia. A case-control study. *Social Psychiatry and Psychiatric Epidemiology* **37**, 329-335.

McCann JB, James SW, Wilson S, Dunn G (1996). Prevalence of psychiatric disorders in young people in the care system. *British Medical Journal* **313**, 1529-1530.

McGuffin P, Farmer A, Harvey I (1991). A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Archives of General Psychiatry* **48**, 764-770.

Morgan C, Abdul-AI R, Lappin JM, Jones P, Fearon P, Leese M, Croudace T, Morgan K, Dazzan P, Craig T, Leff J, Murray R (2006). Clinical and social determinants of duration of untreated psychosis in the AESOP first-episode psychosis study. *British Journal of Psychiatry* **189**, 446-452.

Morgan C, Kirkbride J, Leff J, Craig T, Hutchinson G, McKenzie K, Morgan K, Dazzan P, Doody GA, Jones P, Murray R, Fearon P (2007). Parental separation, loss and psychosis in different ethnic groups: a case-control study. *Psychological Medicine* **37**, 495-503.

Radford L, Corral S, Bradley C, Fisher HL (2013). The prevalence and impact of child maltreatment and other types of victimization in the UK: findings from a population survey of caregivers, children and young people and young adults. *Child Abuse and Neglect* **37**, 801-813.

Read J, Agar K, Argyle N, Aderhold V (2003). Sexual and physical abuse during childhood and adulthood as predictors of hallucinations, delusions and thought disorder. *Psychology & Psychotherapy* **76(Pt 1)**, 1-22.

Read J, Bentall RP (2012). Negative childhood experiences and mental health: theoretical, clinical and primary prevention implications. *British Journal of Psychiatry* **200**, 89-91.

Read J, van Os J, Morrison AP, Ross CA (2005). Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica* **112**, 330-350.

Rutter M (2006). *Genes and Behaviour: Nature-Nurture Interplay Explained*. Blackwell Publishing: Oxford.

Sarchiapone M, Carli V, Cuomo C, Marchetti M, Roy A (2009). Association between childhood trauma and aggression in male prisoners. *Psychiatry Research* **165(1-2)**, 187-192.

Schürhoff F, Laguerre A, Fisher H, Etain B, Méary A, Soussy C, Szöke A, Leboyer M (2009). Self-reported childhood trauma correlates with schizotypal measures in schizophrenia but not bipolar pedigrees. *Psychological Medicine* **39(3)**, 365-370.

Sideli L, Mule A, La Barbera D, Murray RM (2012). Do child abuse and maltreatment increase risk of schizophrenia? *Psychiatry Investigation* **9**, 87-99.

Singh SP, Cooper J, Fisher HL, Tarrant CJ, Lloyd T, Banjo J, Corfe S, Jones P (2005). Determining the chronology and components of psychosis onset: the Nottingham Onset Schedule (NOS). *Schizophrenia Research* **80**, 117-130.

Sitko K, Bentall RP, Shevlin M, O'Sullivan N, Sellwood W (2014). Associations between specific psychotic symptoms and specific childhood adversities are mediated by attachment styles: an analysis of the National Comorbidity Survey. *Psychiatry Research* **217**, 202-209.

Smith PN, Gamble SA, Cort NA, Ward EA, Conwell Y, Talbot NL (2012). The relationships of attachment style and social maladjustment to death ideation in depressed women with a history of childhood sexual abuse. *Journal of Clinical Psychology* **68**, 78-87.

Stefanovics EA, Elkis H, Zhening L, Zhang XY, Rosenheck RA (2014). A cross-national factor analytic comparison of three models of PANSS symptoms in schizophrenia. *Psychiatry Research* **219**, 283-289.

Stilo SA, Di Forti M, Mondelli V, Falcone AM, Russo M, O'Connor J, Palmer E, Paparelli A, Kolliakou A, Sirianni M, Taylor H, Handley R, Dazzan P, Pariante C, Marques TR, Zoccali R, David A, Murray RM, Morgan C (2013). Social disadvantage: cause or consequence of impending psychosis? *Schizophrenia Bulletin* **39**, 1288-1295.

Trotta A, Di Forti M, Iyegbe C, Green P, Dazzan P, Mondelli V, Morgan C, Murray RM, Fisher HL (2015). Familial risk and childhood adversity interplay in the onset of psychosis. *British Journal of Psychiatry Open* **1(1)**, 6-13.

van Os J, Fahy TA, Jones P, Harvey I, Sham P, Lewis S, Bebbington P, Toone B, Williams M, Murray R (1996). Psychopathological syndromes in the functional psychoses: associations with course and outcome. *Psychological Medicine* **26**, 161-176.

van Os J, Gilvarry C, Bale R, Van Horn E, Tattan T, White I, Murray R (1999). A comparison of the utility of dimensional and categorical representations of psychosis. UK700 Group. *Psychological Medicine* **29**, 595-606.

Vassos E, Sham PC, Cai G, Deng H, Liu X, Sun X, Zhao J, Murray RM, Collier DA, Li T (2008). Correlation and familial aggregation of dimensions of psychosis in affected sibling pairs from China. *British Journal of Psychiatry* **193**, 305-310.

Velikonja T, Fisher HL, Mason O, Johnson S (2015). Childhood trauma and schizotypy: a systematic literature review. *Psychological Medicine* **45(5)**, 947-963.

Wallwork RS, Fortgang R, Hashimoto R, Weinberger DR, Dickinson D (2012). Searching for a consensus five-factor model of the Positive and Negative Syndrome Scale for schizophrenia. *Schizophrenia Research* **137**, 246-250.

White L, Harvey PD, Opler L, Lindenmayer JP (1997). The PANSS Study Group Empirical assessment of the factorial structure of clinical symptoms in schizophrenia. *Psychopathology* **30**, 263–274.

Whitfield CL, Dube SR, Felitti VJ, Anda RF (2005). Adverse childhood experiences and hallucinations. *Child Abuse & Neglect* **29(7)**, 797-810.

Wickham S, Sitko K, Bentall RP (2015). Insecure attachment is associated with paranoia but not hallucinations in psychotic patients: the mediating role of negative self-esteem. *Psychological Medicine* **45(7)**, 1495-1507.

World Health Organisation (1992). *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. World Health Organisation: Geneva, Switzerland.

Table 1. *Demographic and clinical characteristics of the sample and distribution of type of childhood adversity*

Characteristics	n (%)
Age at first contact	
Mean (SD)	28.7 (9.1)
Gender	
Female	83 (35.2%)
Male	153 (64.8%)
Ethnicity	
White (all groups)	83 (35.2)
Black (all groups)	95 (40.2)
Other	58 (24.6)
Diagnosis	
Schizophrenia spectrum	154 (68.8%)
Affective psychosis	60 (26.8%)
Other psychotic disorders	10 (4.5)
Death of one or both parents	
No	208 (89.7)
Yes	24 (10.3)
Separation from one or both parents	
No	151 (65.1)
Yes	81 (34.9)
Physical abuse by either or both parents	
No	169 (72.8)
Yes	63 (27.2)
Sexual abuse	
No	207 (87.7)
Yes	29 (12.3)
Taken into care	
No	178 (90.4)
Yes	19 (9.6)

SD, standard deviation.

Table 2. Associations between types of childhood adversity and the Wallwork/Fortgang continuous five-factor psychosis symptom dimension scores

Type of childhood adversity	Negative β (SE) [95% CI]	Positive β (SE) [95% CI]	Excited β (SE) [95% CI]	Depressed β (SE) [95% CI]	Disorganised/concrete β (SE) [95% CI]
Death of one or both parents	0.17 (0.23) [-0.29-0.63]	-0.17 (0.34) [-0.83-0.49]	-0.01 (0.13) [-0.27-0.25]	0.07 (0.15) [-0.22-0.36]	0.19 (0.23) [-0.26-0.64]
Separation from one or both parents	-0.20 (0.16) [-0.52-0.11]	0.51 (0.23)* [0.06-0.96]	0.04 (0.09) [-0.14-0.21]	-0.12 (0.10) [-0.31-0.08]	0.25 (0.15) [-0.06-0.55]
Physical abuse by either or both parents	0.03 (0.16) [-0.29-0.35]	0.62 (0.23)*** [0.18-1.07]	0.20 (0.09)* [0.02-0.37]	-0.02 (0.10) [-0.21-0.18]	0.39 (0.15)** [0.09-0.69]
Sexual abuse	-0.17 (0.21) [-0.57-0.24]	0.90 (0.28)*** [0.34-1.46]	0.22 (0.11)* [0.003-0.45]	0.07 (0.13) [-0.18-0.32]	0.17 (0.20) [-0.22-0.56]
Taken into care	0.16 (0.26) [-0.35-0.66]	0.48 (0.36) [-0.24-1.20]	0.40 (0.14)*** [0.13-0.67]	0.10 (0.16) [-0.21-0.42]	0.49 (0.24)* [0.01-0.97]

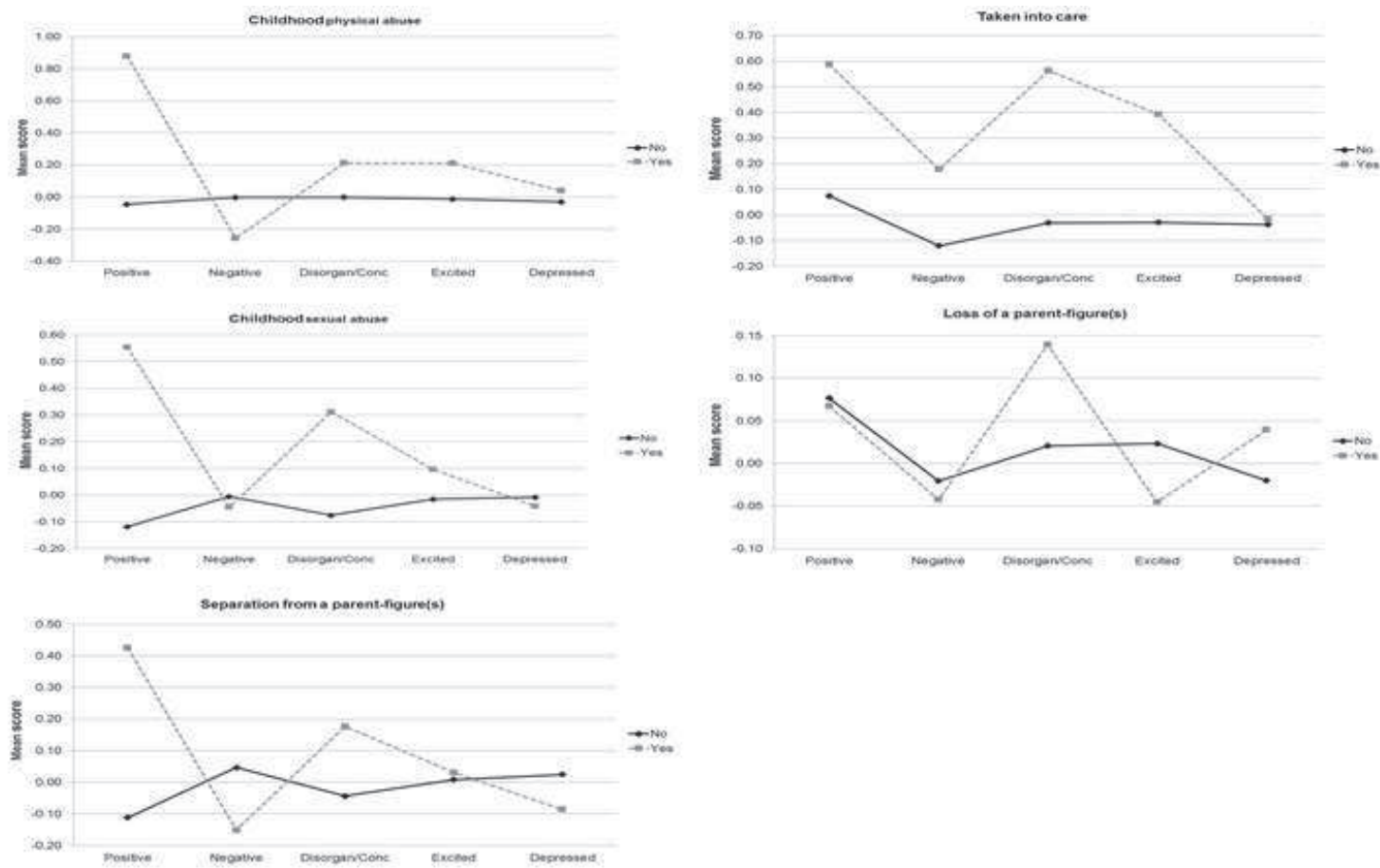
*p<0.05, ** p<0.01, *** p<0.001. β, unstandardized linear regression coefficient. CI, confidence intervals. SE, standard error.

The analyses are controlled for age at the time of first contact with mental health services for psychosis, gender, ethnicity, lifetime use of substances (alcohol, cannabis and other illegal substances) prior to onset of psychosis, and family history of psychosis.

Figure legends

Fig. 1 Graphs display the mean psychosis symptom dimension scores for each type of childhood adversity among first-episode psychosis patients. The continuous symptom dimension scores were derived using the 'predict' post-estimation command in Stata following a confirmatory factor analysis of the Wallwork/Fortgang five-factor model (Wallwork *et al.* 2012) of the items from the Positive and Negative Syndrome Scale (Kay *et al.*, 1987). The five dimensions capture positive, negative, disorganised/concrete (disorgan/conc), excited, and depressed symptom items at first presentation to psychiatric services. Childhood adversities reported by patients as occurring prior to 17 years of age have been dichotomised into 'yes' (present) versus 'no' (absent) according to published guidelines (Bifulco *et al.* 2005).

Figure(s)
Click here to download Figure(s): O Ajnakina et al Fig 1 Final.tif



Supplementary Table 1. Comparisons of demographic and clinical characteristics between psychosis patients in the GAP sample who did and did not complete the PANSS

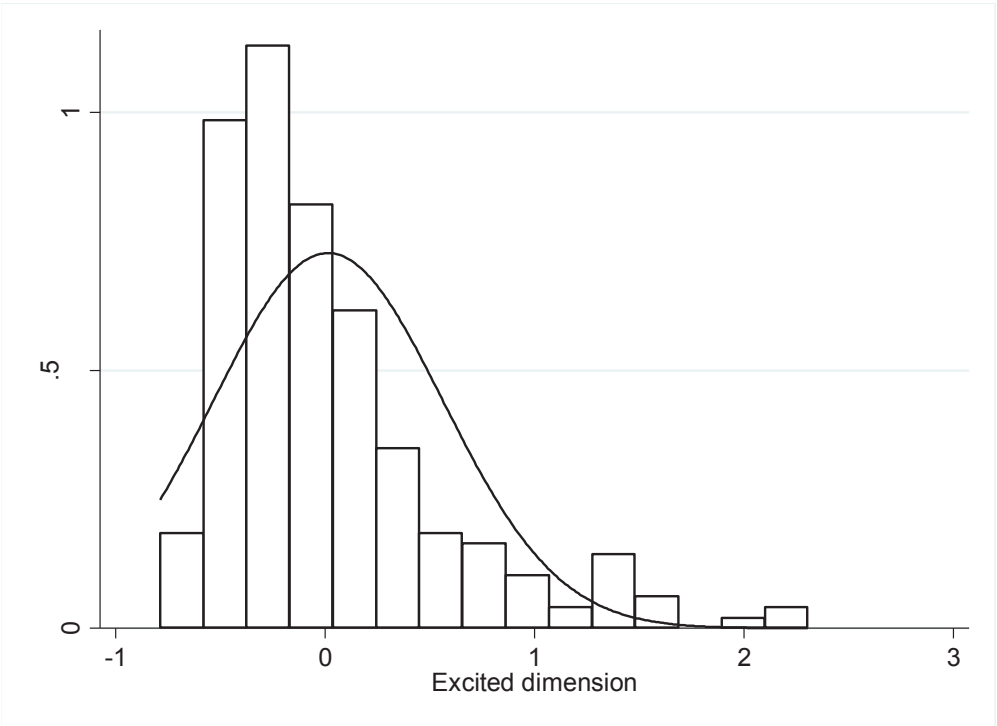
Characteristics	Completed PANSS	Not completed PANSS	Test statistic
	(N=236; 69.6%) n (%)	(N=103; 30.4%) n (%)	
Age at first contact			
Mean (SD)	29.0 (9.1)	33.7 (10.6)	$t=1.97, p=0.05$
Gender			
Female	77 (35.8)	43 (39.4)	$\chi^2=0.41; p=0.52$
Male	138 (64.2)	66 (60.6)	
Ethnicity			
White (all groups)	83 (35.2)	51 (42.9)	$\chi^2=2.25, p=0.33$
Black (all groups)	95 (40.2)	40 (33.6)	
Other	58 (24.6)	28 (23.5)	
Diagnosis			
Schizophrenia spectrum	142 (68.3)	59 (62.8)	$\chi^2=3.29; p=0.19$
Affective psychosis	57 (27.4)	26 (27.7)	
Other psychotic disorders	9 (4.3)	9 (9.6)	

GAP, Genetics and Psychosis study. PANSS, Positive and Negative Syndrome Scale. SD, standard deviation.

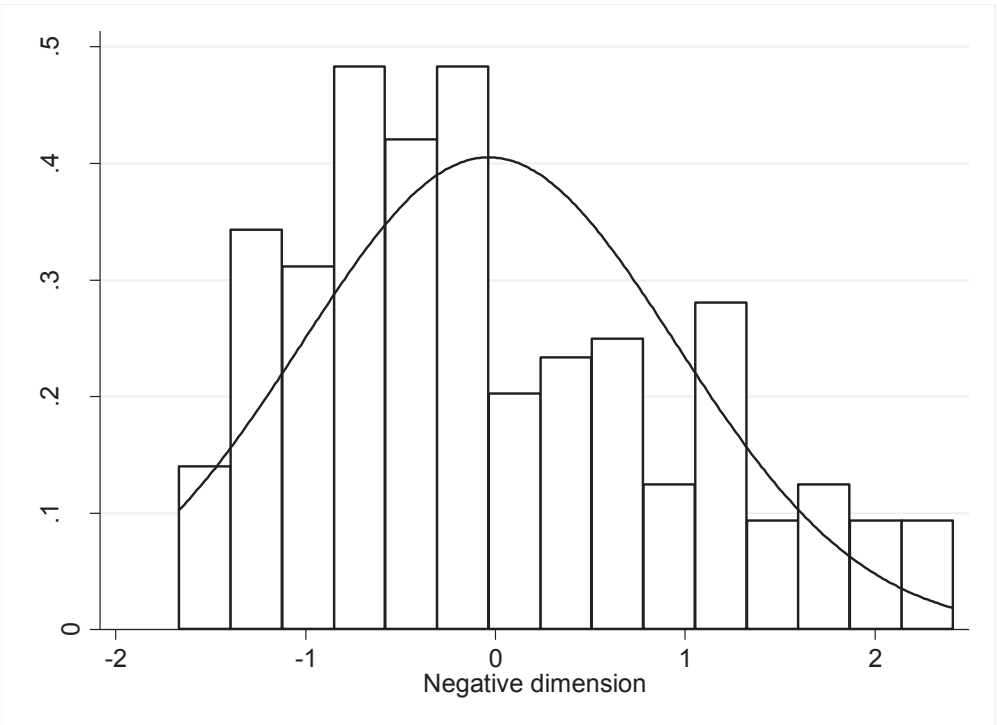
Supplementary Table 2. Mean and standard deviation (SD) of PANSS scores for the GAP sample

	PANSS items	Mean (SD)
P1	Delusions	3.07 (1.76)
P2	Conceptual disorganisation	2.11 (1.33)
P3	Hallucinatory behaviour	2.51 (1.79)
P4	Excitement	1.75 (1.22)
P5	Grandiosity	1.97 (1.49)
P6	Suspiciousness/persecution	2.74 (1.66)
P7	Hostility	1.53 (0.94)
N1	Blunted affect	2.14 (1.42)
N2	Emotional withdrawal	2.19 (1.25)
N3	Poor rapport	1.74 (1.06)
N4	Passive/apathetic social withdrawal	2.28 (1.42)
N5	Difficulty in abstract thinking	2.80 (1.56)
N6	Lack of spontaneity & flow of conversation	2.26 (1.48)
N7	Stereotyped thinking	1.96 (1.24)
G1	Somatic concern	1.71 (1.14)
G2	Anxiety	2.51 (1.25)
G3	Guilt feelings	1.91 (1.37)
G4	Tension	1.91 (1.12)
G5	Mannerisms & posturing	1.21 (0.65)
G6	Depression	2.75 (1.47)
G7	Motor retardation	1.67 (1.06)
G8	Uncooperativeness	1.35 (0.74)
G9	Unusual thought content	2.16 (1.45)
G10	Disorientation	1.44 (0.84)
G11	Poor attention	1.82 (1.06)
G12	Lack of judgement & insight	3.29 (1.74)
G13	Disturbance of volition	1.55 (0.93)
G14	Poor impulse control	1.54 (1.05)
G15	Preoccupation	2.17 (1.30)
G16	Active social avoidance	2.25 (1.37)

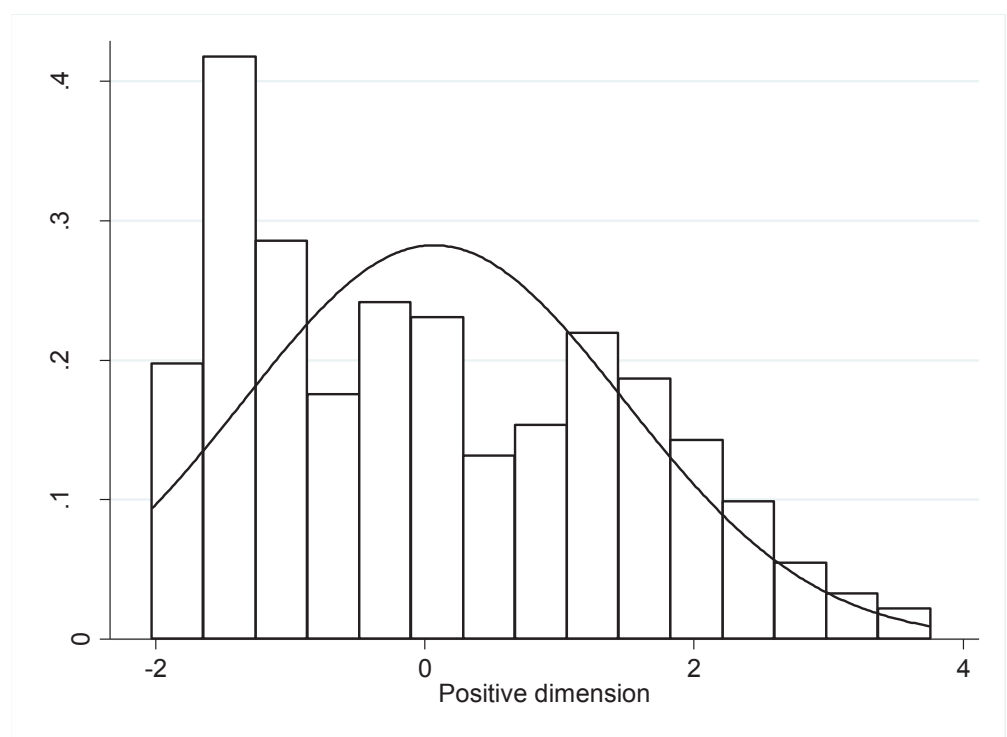
GAP, Genetics and Psychosis study. PANSS, Positive and Negative Syndrome Scale.



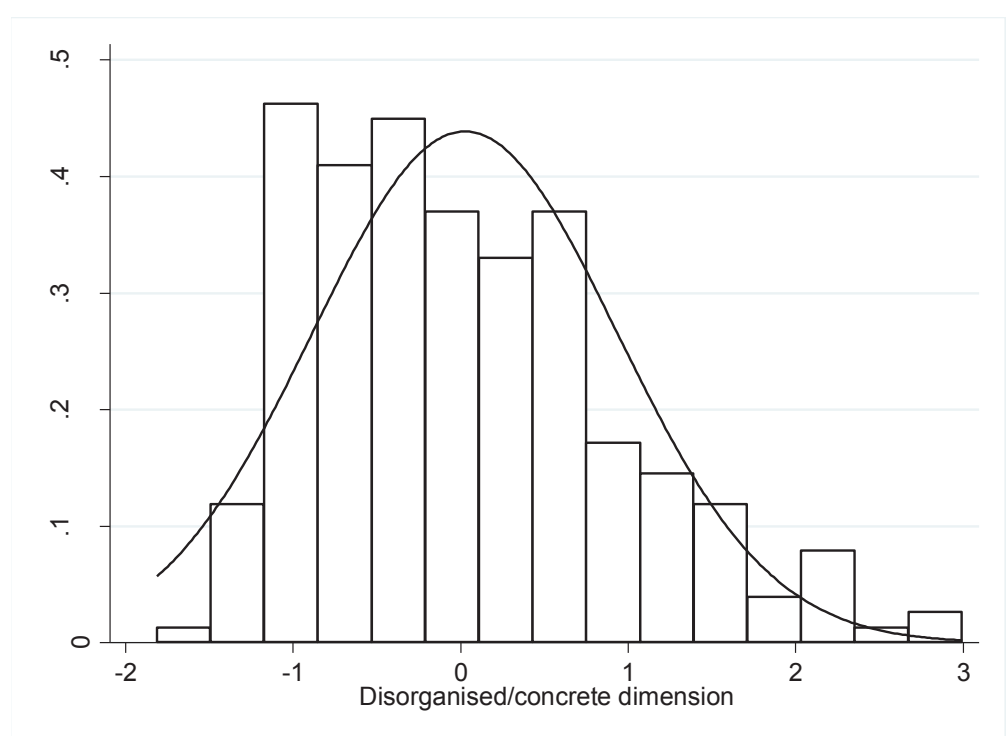
Supplementary Figure 1. *Distribution of the excited dimension scores*



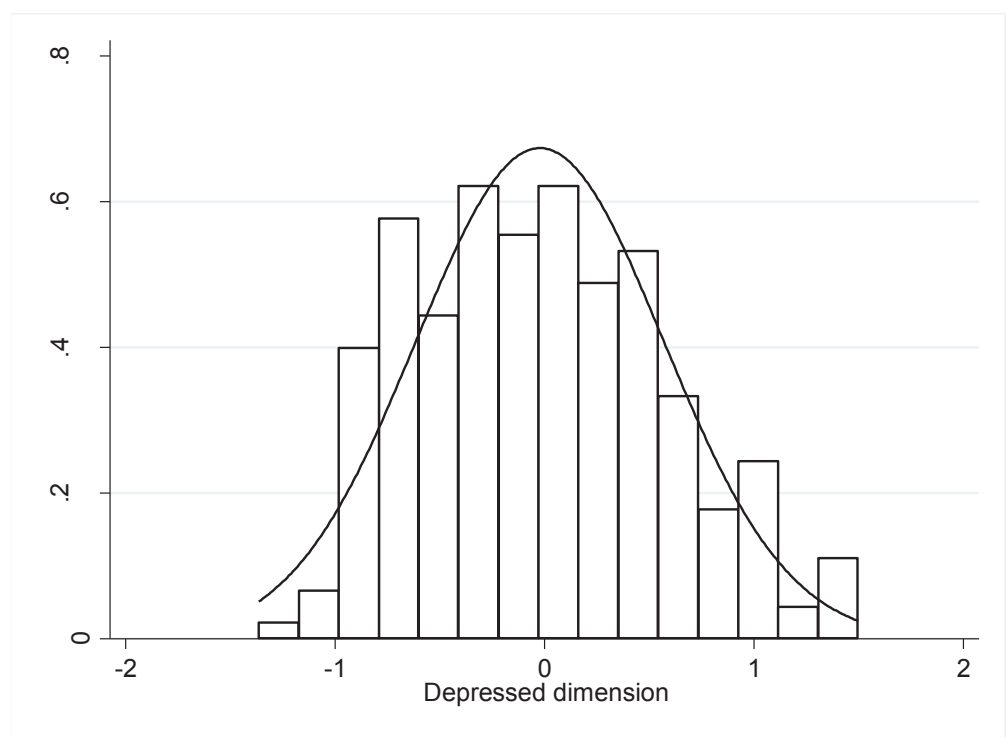
Supplementary Figure 2. *Distribution of the negative symptom dimension scores*



Supplementary Figure 3. *Distribution of the positive symptom dimension scores*



Supplementary Figure 4. *Distribution of the disorganised/concrete symptom dimension scores*



Supplementary Figure 5. *Distribution of the depressed symptom dimension scores*